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Date:
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ARCADIS Project No.:
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Subject:
Toxicological Assessment of Potential Intermediates of Sulfolane Breakdown

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This memo presents an assessment of the toxicological properties of potential degradation intermediates of sulfolane. Several compounds have been identified as potential biotic or abiotic intermediates of sulfolane. It is not known if these intermediates are formed or, if they were formed, whether they would be stable in the environment. ARCADIS reviewed toxicological data on these compounds and on analogous compounds to determine if any information was available on the toxicity of the structures. Data search methods and the results of the review are presented below. In the absence of toxicological data, ARCADIS completed predictive toxicological modeling to predict their toxicological properties, a summary of which is also provided below.

Toxicological Data Search Methods

Toxicological properties were searched by several methods, including searching the following:

- Global Portal to Information on Chemical Substances
- eChemPortal (www.echemportal.org), which contains information from 27 international databases
- European Chemicals Agency (ECHA) Information on Chemicals database (echa.europa.eu)
- National Library of Medicine's PubMed database
- Toxnet (toxnet.nlm,nih.gov)
- International Programme on Chemical Safety (IPCS), Evaluations of the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert

Committee on Food Additives (JECFA) (http://apps.who.int/ipsc/database/evaluations/search.aspx).

Toxicological Predictive Modeling

When toxicological data were not found, two computational toxicology models were executed to predict the toxicological properties of potential intermediates of sulfolane - the Lazy Structure Activity Relationship (LAZAR) model and the Virtual Models for the Evaluation of Chemicals within a Global Architecture Non-Interactive Client (VEGA-NIC) version 1.0.6.

LAZAR

The LAZAR online toxicity prediction model (http://lazar.in-silico.de/predict) is a model based on OpenTox (http://www.opentox.org/) services. It is developed by in silico toxicology GmbH. The model contains the following toxicological prediction modules:

- Carcinogenicity
  - Distributed Structure-Searchable Toxicity (DSSTox) Carcinogenic Potency DBS Hamster
  - DSSTox Carcinogenic Potency DBS Mouse
  - DSSTox Carcinogenic Potency DBS MultiCellCall
  - DSSTox Carcinogenic Potency DBS Rat
  - DSSTox Carcinogenic Potency DBS SingleCellCall
  - DSSTox ISSCAN v3a Canc
- Mutagenicity:
  - DSSTox Carcinogenic Potency DBS
  - Mutagenicity
  - Kazius-Bursi Salmonella mutagenicity
- Repeated Dose Toxicity
- U.S. Food and Drug Administration (USFDA) v3b Maximum Recommended Daily Dose (MRDD) (millimol [mmol])

The output for each chemical provides the prediction for each model (e.g., carcinogen, non-carcinogen, mutagen, non-mutagen, MRDD) along with the confidence score, which indicates the applicability domain of the model. Confidence values range from 0 to 1 (with higher values indicating higher prediction reliability). According to the software documentation, a confidence rating 0.025 or higher indicates a reliable prediction. Helma (2005) performed a validation study of LAZAR predictions using a confidence value of 0.05 as a cutoff for reliability. Thus, the confidence rating varies according to user needs. Rationales for predictions, applicability domain estimations, and validation results are presented in the model output.

The LAZAR tool predicts the MRDD from the USFDA's Center for Drug Evaluation and Research, Office of Pharmaceutical Science, Informatics and Computational Safety Analysis MRSS database. The MRDD database contains values for over 1,200 pharmaceuticals listed in Martindale: The Extra Pharmacopoeia (Blacow 1972, Wade 1982, Reynolds 1993) and The Physicians' Desk Reference (Medical Economics 1995, 1999). Most of the MRDD values in the database were determined from pharmaceutical clinical trials that employed an oral route of exposure and daily treatments, usually for 3 to 12 months.

The MRDD is equivalent to a No Observed Adverse Effect Level (NOAEL) in humans. A risk-based drinking water criterion can be derived by applying regulatory safety factors (10 for subchronic to chronic exposures and 10 for intraspecies sensitivity) and assuming a 2-liters-per-day exposure to drinking water. These risk-based criteria can be compared to the U.S. Environmental Protection Agency (EPA) Regional Screening Level (RSL) for sulfolane of 0.016 milligrams per liter (mg/L) and a screening level derived using the sulfolane alternative cleanup level (ACL) of 0.014 mg/L.

In addition, LAZAR also predicts carcinogenicity using six DSSTox carcinogenicity databases. Again, confidence ratings of 0.025 or higher indicate reliable predictions according to LAZAR documentation, but others have designated 0.05 as a reliability cut-off value.

VEGA-NIC

Additionally, the VEGA-NIC version 1.0.6 was used to predict whether sulfolane's predicted potential break-down intermediate products are mutagenic, carcinogenic or developmental toxicants. VEGA-NIC contains the following models:

- Mutagenicity model (CAESAR v2.1.10)
  - Quantitative structure-activity relationship (QSAR) classification based on a Support Vector Machine combined by a set of ToxTree rules developed by Benigni/Bossaare
- Mutagenicity model (SarPy model v.1.0.5-BETA)
  - QSAR classification model based on rules set by the SarPy software
- Carcinogenicity model (CAESAR v.2.1.6)
  - Results are assigned as either positive and non-positive; compound is assigned to the class having value >0.5
  - Structural alerts from ToxTree are provided (if any)
- Developmental toxicity model (CAESAR v2.1.4)
  - QSAR classification model for Developmental Toxicity based on a Random Forest classification

Queries and Reliability

Each model first searches for experimental data contained within its dataset. If no experimental data are located for the queries compound, it then searches for data for compounds within the same applicability

domain. The model provides the reliability of each prediction, which generally falls into the following categories:

- Good reliability:
  - Match between prediction and experimental data
- Result shows some critical aspects, which require to be checked:
  - Compound could be out of model applicability domain (model flags the result to be checked by the user)
- Result may not be reliable:
  - Compound is out of model applicability domain

For each queried compound, the model shows similar compounds within the applicability domain, each compound's similarity to the queried compound (ranging from 0 to 1) and their experimental and predicted values.

Assessment Results

The table below provides the assessment results for sulfolane, the potential intermediates of aerobic biodegradation, and the potential intermediates of aerobic abiotic reactions. The results indicate that the potential intermediates all have lower toxicity than sulfolane. More specific modeling results are provided in the attached Table 1.

1. Sulfolane (CAS #126-33-0)

Toxicological data exist for sulfolane, and EPA has issued a Provisional Peer-Reviewed Toxicity Value (PPRTV) for Sulfolane of 0.001 milligrams per kilogram per day (mg/kg-day) using the NOAEL for reduction of white blood cells in rats in the Huntingdon Life Sciences study (HLS, 2001). Based on the chronic PPRTV, EPA derived a RSL for drinking water of 0.016 mg/L. As explained in the ARCADIS Scenario of the Revised Draft Final Human Health Risk Assessment (HHRA) submitted on May 23, 2012 (ARCADIS 2012), this is at the low end of a range of health protective values. As explained in Appendix K to the HHRA, there are many reasons why sulfolane is best evaluated through a careful and specific assessment of the toxicology data, which provides a picture of sulfolane as a minimally toxic chemical at low levels in a variety of animal test systems.

There is no need to perform predictive modeling for sulfolane, and predictive modeling cannot replace the careful assessment of the available toxicology data as part of a risk assessment process, but the LAZAR and VEGA-NIC models were executed to determine how well the predictions would match the toxicological analysis reflected in the HHRA for sulfolane. Both models predicted with good reliability that sulfolane is not mutagenic. LAZAR also predicted that sulfolane is not carcinogenic. LAZAR also predicted a MRDD of 0.0391 mmol with good confidence. This predicted human NOAEL is equivalent to 4.7 milligrams per day (mg/day). By applying a composite Uncertainty Factor of 100, a reference dose- (RfD-)

like value can be derived from the MRDD, and a risk-based drinking water concentration can be then derived assuming 2 liters (L) of water consumption per day. The risk-based concentration predicted from the specific FDA database of pharmaceutical compounds used by the LAZAR model is 0.0235 mg/L, as compared to the EPA RSL (EPA, 2012) of 0.016 mg/L. Thus, the LAZAR predicted MRDD for sulfolane is within the range of drinking water criteria previously derived by various organizations for sulfolane.

I. Potential Intermediates of Aerobic Biodegradation

1. 4-Hydroxybutane sulfinic acid (CAS #785010-16-4) (1-Butanesulfinic acid, 4-hydroxy-)

No toxicology data were found for this compound. The LAZAR model predicted a human MRDD of 0.194 mmol with a confidence of 0.1. The predicted risk-based concentration in drinking water is 0.13 mg/L. LAZAR also predicted that this compound is not carcinogenic. Six of six predictions were negative. The VEGA-NIC model predicted that this compound is neither mutagenic nor carcinogenic, although both predictions have low reliability ratings. A potential analog of gamma butyric acid was identified. LAZAR predicted 0.393 mmol with a confidence of 0.604. The predicted risk-based concentration in drinking water is 0.27 mg/L. Another potential analog is butyric acid (CAS #107-92-6). Butyric acid is a food additive with no safety concerns (JECFA 1999).

2. Butanol

This compound has an Alaska Department of Environmental Conservation (ADEC) RSL of 3.7 mg/L in drinking water (ADEC 2008). As a food additive, butanol has no safety concerns (JECFA 1999).

3. Butyraldehyde

This compound has no EPA RSL, but an RSL exists for the structurally similar compound, propionaldehyde, at 0.018 mg/L. As a food additive, propionaldehyde has no safety concerns (JECFA 1999).

4. Butanoic acid

Butanoic acid (butyric acid) is a food additive with no safety concerns (JECFA 1999).

II. Potential Intermediates of Aerobic Abiotic Reactions

1. 4-Hydroxybutane sulfinic acid (CAS #785010-16-4) (1-Butanesulfinic acid, 4-hydroxy-) (4-Hydroxybutane sulfinate)

No toxicology data were found for this compound. The LAZAR model predicted 0.194 mmol with a confidence of 0.1. The predicted risk-based concentration in drinking water is 0.13 mg/L. LAZAR also predicted that this compound is not carcinogenic. In fact, six of six predictions were negative. A potential analog of gamma butyric acid was identified. LAZAR predicted 0.393 mmol with a confidence of 0.604. The predicted risk-based concentration in drinking water is 0.27 mg/L. Another potential analog is butyric acid (CAS #107-92-6). Butyric acid is a food additive with no safety concerns (JECFA 1999).

2. Butane-1-sulfinic acid (Butanesulfinate)

No toxicology data were found for this compound. The LAZAR model predicted a MRDD of 0.194 mmol with a confidence of 0.1. The predicted risk-based concentration in drinking water is 0.12 mg/L. LAZAR also predicted that this compound is not carcinogenic. Six of six predictions were negative.

3. bis-1,8-octanedisulfinate (Octane-1,8-disulfinate)

No toxicology data were found for this compound. The LAZAR model predicted a MRDD of 0.126 mmol with a confidence rating of 0.1. The predicted risk-based concentration in drinking water is 0.15 mg/L. LAZAR also predicted that this compound is not carcinogenic. Six of six predictions were negative.

3a. Carboxylic acid analog of bis-1,8-octanedisulfinate: 1,10-decanedioic acid (sebacic acid) (CAS #111-20-6)

Sebacic acide is a carboxylic acid analog of bis-1,8-octanedisulfinate and is registered under the European Community Regulation on chemicals and their safe use, known as the Registration, Evaluation, Authorization and Restriction of Chemical substances (REACH), (ECHA 2012). The acute oral Lethal Dose (50%) (LD50) in rats and rabbits exceeds 5,000 milligrams per kilogram (mg/kg). The dermal LD50 in rats exceeds 2000 mg/kg. The repeated dose toxicity studies in rats and rabbits showed No Observed Adverse Effect Levels (NOAELS) from >1,000 mg/kg-day to >4,814 mg/kg-day. Developmental toxicity studies in rabbits and rats showed NOAELs in excess of 500 mg/kg-day. All of these studies demonstrate that sebacic acid has a low order of mammalian toxicity. The LAZAR model also predicted that this compound is not carcinogenic. Five of six predictions were negative. The one positive prediction had a confidence value of 0.04, which is very low. The VEGA-NIC model predicted that the compound is not mutagenic with good confidence.

4. 1-Octanesulfinic acid (Octane-1-sulfinate)

No toxicology data were found for this compound. The LAZAR model predicted an MRDD of 0.05 mmol with a confidence rating of 0.123. The predicted risk-based concentration in drinking water is 0.045 mg/L. LAZER also predicted that this compound is not carcinogenic. Four of six predictions were negative with

high reliability ratings. One was negative with a low reliability rating. One was outside the range of chemicals in the training set.

5. 8-hydroxyoctane sulfinic acid (8—hydroxy octanesulfinate)

No toxicology data were found for this compound. The LAZAR model predicted a MRDD of 0.129 mmol with a confidence rating of 0.157. The predicted risk-based concentration in drinking water is 0.13 mg/L.. LAZER also predicted that this compound is not carcinogenic. Five of six predictions were negative. One prediction was outside the range of chemicals in the training dataset.

6. Octanol

1-, 2-, and 3-octanol are all food additives with no safety concerns (JECFA 1999).

Summary

ARCADIS has summarized the known toxicological data on chemical structures that have been identified as possible intermediates of sulfolane breakdown by aerobic biological or abiotic processes. When toxicological data were unavailable, the LAZAR and VEGA-NIC predictive toxicological models were executed. In all cases, the possible intermediates were known or predicted to be less toxic than sulfolane.

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Acronyms

ACL	Alternative cleanup level
ADEC	Alaska Department of Environmental Conservation
DSSTox	Distributed Structure-Searchable Toxicity
ECHA	European Chemicals Agency
EPA	U.S. Environmental Protection Agency
HLS	Huntingdon Life Sciences
IPCS	International Programme on Chemical Safety
JECFA	Joint FAO/WHO Expert Committee on Food Additives
L	liter
LAZAR	Lazy Structure Activity Relationship
mg/day	milligrams per day
mg/kg	milligrams per kilogram
mg/kg-day	milligrams per kilogram per day
mg/L	milligrams per Liter
mmol	millimol
MRDD	Maximum Recommended Daily Dose
NOAEL	No Observed Adverse Effect Level
PPRTV	Provisional Peer Reviewed Toxicity Value
QSAR	Quantitative Structure-Activity Relationship
REACH	Registration, Evaluation, Authorization and Restriction of Chemical substances
RfD	reference dose
RSL	Regional Screening Level
TRS	Technical Report Series
USFDA	U.S. Food and Drug Administration

VEGA-NIC	Virtual Models for the Evaluation of Chemicals within a Global Architecture Non-Interactive Client
WHO	World Health Organization

Table 1. Predictive Modeling Results

Substance Name	CAS No.	Molecular Formula	Mol. Weight (amu)	Lazar Carcinogenicity/Mutagenicity Predictions	VEGA Non-Interactive Client v.1.0.6 Mutagenicity / Carcinogenicity / Developmental Toxicity Predictions	Predicted Human Toxicity Threshold	MRDD/ 100 (mmol)†‡	MRDD/ 100 (mg)	DW Conc. (mg/L)#
Sulfolane	126-33-0	$C_4H_8O_2S$	120.17	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.0198) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0596) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0643) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0333) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.117) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0754) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (measured activity)	Mutagenicity: non-mutagen (good reliability) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: NOEL: 60 mg/kg bw/day (rat) Lazar: FDA v3b MRDD: 0.0391 (Confidence: 0.121)	3.91E-04	4.70E-02	2.35E-02
4-Hydroxybutane-1-sulfinic acid	785010-16-4	$C_4H_{10}O_3S$	138.19	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.0486) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0652) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0479) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0151) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.0646) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0865) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0406)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: No data Lazar: FDA v3b MRDD: 0.194 (Confidence: 0.0847)	1.94E-03	2.68E-01	1.34E-01
Butane-1-sulfinic acid (butane sulfinate)	5675-04-744602-11-1	$C_4H_{10}O_2S$	122.19	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.00557) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0461) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0135) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0333) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.111) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0832) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0687)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox:No data Lazar:FDA v3b MRDD: 0.194 mmol (Confidence: 0.0847)	1.94E-03	2.37E-01	1.19E-01
bis-1,8-Octanedisulfinate (octane-1,8-disuflinate)	N/A	$C_8H_{18}O_4S_2$	242.36	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.00557) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0461) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0135) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0333) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.111) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0832) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0687)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: No data Lazar: FDA v3b MRDD: 0.126 mmol (Confidence: 0.137)	1.26E-03	3.05E-01	1.53E-01

Table 1. Predictive Modeling Results

Substance Name	CAS No.	Molecular Formula	Mol. Weight (amu)	Lazar Carcinogenicity/Mutagenicity Predictions	VEGA Non-Interactive Client v.1.0.6 Mutagenicity / Carcinogenicity / Developmental Toxicity Predictions	Predicted Human Toxicity Threshold	MRDD/ 100 (mmol)†‡	MRDD/ 100 (mg)	DW Conc. (mg/L)#
bis-1,10-Decanedisulfinate	99868-37-8	$C_{10}H_{22}O_4S_2$	270.41	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.00557) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0461) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0135) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0333) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.111) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0832) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0687)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: No data Lazar: FDA v3b MRDD: 0.03 mmol (Confidence: 0.14)	3.00E-04	8.11E-02	4.06E-02
1,10-Decanedioic acid (sebacic acid)	111-20-6	$C_{10}H_{18}O_4$	202.25	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.12) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0861) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0995) DSSTox ISSCAN v3a Canc: carcinogen (0.0442) DSSTox Carcinogenic Potency DBS Hamster: non-carcinogen (0.769) DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.163) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.156) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (measured activity)	Mutagenicity: Model assessment: Experimental activity is NON-Mutagen; Model prediction is NON-Mutagen (good reliability) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: Ames test (*S. typhimurium*): negative Lazar: FDA v3b MRDD: 0.106 mmol (Confidence: 0.164)	1.06E-03	2.14E-01	1.07E-01
8-Hydroxyoctane sulfinic acid	N/A	$C_8H_{18}O_3S$	194.29	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.0486) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0652) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0479) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0151) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.646) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0865) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0406)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: No data Lazar: FDA v3b MRDD: 0.129 mmol (Confidence: 0.157)	1.29E-03	2.51E-01	1.25E-01
1-Octanesulfinic acid	NA	$C_8H_{18}O_2S$	178.29	DSSTox Carcinogenic Potency DBS MultiCellCall: non-carcinogen (0.00557) DSSTox Carcinogenic Potency DBS Rat: non-carcinogen (0.0461) DSSTox Carcinogenic Potency DBS SingleCellCall: non-carcinogen (0.0135) DSSTox ISSCAN v3a Canc: non-carcinogen (0.0333) DSSTox Carcinogenic Potency DBS Hamster: Not enough similar compounds in training dataset. DSSTox Carcinogenic Potency DBS Mouse: non-carcinogen (0.111) DSSTox Carcinogenic Potency DBS Mutagenicity: non-mutagenic (0.0832) Kazius-Bursi Salmonella mutagenicity: non-mutagenic (0.0687)	Mutagenicity: non-mutagen (compound is out of model applicability domain) (both models) Carcinogenicity: non-carcinogen (compound is out of model applicability domain) Developmental toxicity: developmental toxicant (compound is out of model applicability domain)	QSAR Toolbox: No data Lazar: FDA v3b MRDD: 0.050 mmol (Confidence: 0.123)	5.00E-04	8.91E-02	4.46E-02

† Maximum Recommended Daily Dose

‡ The MRDD is equivalent to a No Observed Adverse Effect Level (NOAEL) in humans. A risk-based drinking water criterion can be derived by applying regulatory safety factors (10 for subchronic to chronic exposures and 10 for intraspecies sensitivity).

Drinking water concentrations were calculated assuming 2 L per person per day. These risk-based criteria can be compared to the EPA Regional Screening Level for sulfolane of 0.016 mg/L.

Green font indicates predictions that are within model applicability range and with confidence values >0.025.